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<b>(21) International Application Number:</b> PCT/US96/05378 <b>(22) International Filing Date:</b> 18 April 1996 (18.04.96)  <b>(30) Priority Data:</b> 08/467,099                      6 June 1995 (06.06.95)                      US  <b>(71) Applicant:</b> MAXDEM INCORPORATED [US/US]; 140 East Arrow Highway, San Dimas, CA 91773 (US).  <b>(72) Inventors:</b> WANG, Ying; 23637 Country View Drive, Diamond Bar, CA 91765 (US). MARROCCO, Matthew, L., III; 2418 North French Street, Santa Ana, CA 92703 (US). TRIMMER, Mark, S.; 144 North Lincoln Place, Monrovia, CA 91016 (US).  <b>(74) Agents:</b> CHRISTIE, William, P. et al.; Christie, Parker & Hale, P.O. Box 7068, Pasadena, CA 91109-7068 (US).		<b>(81) Designated States:</b> CA, JP, KR, European patent (AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE).  <b>Published</b> <i>With international search report.</i> <i>With amended claims.</i>
<b>(54) Title:</b> NICKEL PHOSPHITE CATALYSTS  <b>(57) Abstract</b>  Methods for coupling aryl halides or aryl sulfonates to produce biaryls or polyaryls using novel nickel phosphite catalysts are provided.		

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## NICKEL PHOSPHITE CATALYSTS

Field of the Invention:

This invention relates to nickel phosphite catalysts for coupling aryl halides or aryl sulfonates to produce biaryls or polyaryls.

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Background of the Invention:

The coupling of aryl compounds to form biaryl compounds or polyaryl compounds via carbon-carbon bonds is of great synthetic importance. A large number of methods are known to effect such couplings, including Ullman couplings of aryl iodides and bromides (see P.E. Fanta, "The Ullman Synthesis of Biaryls," *Synthesis*, 9, 9-21, 1974), coupling of aryl bromides and iodides with aryl boronic acids and esters using palladium catalysts (A. Suzuki, *Acc. Chem. Res.*, 15, 178, 1982), reductive coupling of aryl halides with magnesium via Grignard reagents using nickel catalysts (T. Yamamoto and A. Yamamoto, *Chem. Lett.*, 353-356, 1977), reductive coupling of aryl chlorides with zinc using nickel triphenylphosphine catalysts (I. Colon and D.R. Kelsey, *J. Org. Chem.*, 51, 2627-2637, 1986; and U.S. Patent No. 4,326,989) and oxidative coupling of phenols using iron

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1 (III) or air and copper catalysts (L. F. Fieser and M.  
Fieser, Reagents for Organic Synthesis, Vol. 1, 390,  
1967) ..

5 Each of the above-referenced prior art methods for  
the coupling of aryl compounds has certain limitations.  
The Ullman coupling generally results in low yields and,  
for best results, requires aryl iodides, which are  
expensive. Although coupling of aryl chlorides, which are  
10 less expensive than aryl iodides and aryl bromides, has  
been accomplished by Yamamoto et al via Grignard reagents,  
the generally more expensive aryl bromides and iodides are  
preferred. In addition, in the Yamamoto et al coupling  
reactions, groups such as ketones and esters, which are  
15 not stable to Grignard conditions, must be avoided,  
thereby limiting the scope of useful reactions. While the  
Suzuki coupling is the method of choice for cross-coupling  
to form asymmetric biaryls, it uses expensive palladium  
catalysts and boronic acid substrates, which makes the  
process more expensive and, hence, less desirable.

20 Because aryl chlorides cost substantially less than  
aryl bromides and aryl iodides, the nickel phosphine  
catalyzed couplings disclosed by Colon et al are widely  
used. In the Colon et al method, a nickel compound, salt,  
or complex is reduced in situ with zinc powder in the  
25 presence of a phosphine (specifically a triaryl phosphine)  
to form an active nickel (0) phosphine catalyst. It is  
theorized that in the triarylphosphine process, each of  
the nickel species in the catalytic cycle is capable of  
losing one or more of its phosphine ligands (L) to form  
30 coordinatively unsaturated complexes. These equilibria  
have been studied by Tolman (C.A. Tolman, W.C. Seidel, and  
L.W. Gosser, *J. Am. Chem.*, 96, 53 (1974)). The formation  
of unsaturated complexes is said to be essential at certain

1 parts of the cycle, so that the aryl halide may react.  
However, during other parts of the cycle, unsaturated  
nickel complexes may cause the formation of unwanted by-  
products or may react to form inert complexes unable to  
5 catalyze further coupling. It has been found in using  
the Colon et al process that the concentration of  
phosphine ligand must be kept between certain limits to  
prevent the formation of unsaturated nickel complexes  
which are too reactive and which lead to unwanted side  
10 reactions. The typical range of concentrations is  
approximately 0.2 to 0.5 M triphenylphosphine, 0.5 to 1 M  
aryl halide, and 0.01 to 0.05 M nickel.

In view of the foregoing, it can be seen that in the  
Colon et al. process relatively large amounts of  
15 triphenylphosphine must be used in coupling reactions  
compared to the amount of aryl halide substrate. Since  
such large amounts of triphenylphosphine must be used,  
recovery and purification of triphenylphosphine is  
required to enhance process economics. Because of the  
20 inefficiencies involved in the recovery, the cost of the  
process is substantially increased.

In addition to the increased cost of the Colon et al  
process due to the loss of triphenylphosphine, such  
processes also result in unwanted by-products due to  
25 abstraction of an aryl group ( $Ar'$ ) from the phosphine  
 $P(Ar')_3$ . The abstracted aryl group can couple to aryl  
halide ( $ArX$ ), giving an undesired by-product  $Ar-Ar'$ , for  
example. While increasing the concentration of phosphine  
ligand can suppress (but not eliminate) this undesired  
30 side reaction, increasing the phosphine concentration  
further increases the loss of triphenylphosphine, thereby  
increasing the overall process cost.

1 Aryl sulfonates react in a fashion similar to aryl  
halides and may be coupled using nickel phosphine  
catalysts such as that of Colon et al., for example, see  
the work of Percec et al. (V. Percec, J-Y. Bae, M. Zhao,  
5 and D. H. Hill, *J. Org. Chem.*, 1995, 60, 176-185; and U.  
S. 5,241,044, issued August 31, 1993.)

There is a need in the art for economical catalyst  
systems which can be used in reactions which couple aryl  
halides or aryl sulfonates to form either biaryl or  
10 polyaryl compounds and which enhance the economics of the  
process while reducing or substantially eliminating by-  
product formation.

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1     Summary of the Invention:

          An economical method for coupling aryl halides or  
aryl sulfonates to form biaryl or polyaryl compounds is  
provided which minimizes by-product formation. The method  
5     comprises the steps of (1) providing an aryl sulfonate  
non-limiting examples of which include an aryl  
methanesulfonate (aryl mesylate), an aryl  
trifluoromethanesulfonate (aryl triflate), an aryl  
phenylsulfonate, an aryl tolylsulfonate (aryl tosylate),  
10    an aryl fluorosulfonate, and an aryl  
fluorophenylsulfonate; or an aryl halide selected from the  
group consisting of an aryl chloride, an aryl bromide, and  
an aryl iodide, (2) contacting the aryl sulfonate or aryl  
15    halide in an anhydrous aprotic solvent with a catalyst  
mixture comprising a nickel compound or complex, a  
phosphite ligand, and a reducing metal to thereby form the  
biaryl or polyaryl compound.

          The coupled products provided in accordance with this  
invention can be used, inter alia, as monomers for  
20    subsequent polymerization, as high boiling heating fluids,  
as plasticizers for plastics and as chemicals in  
pharmaceutical intermediates.

          In one preferred embodiment of the present invention,  
the aryl halide has the formula:



          wherein X is independently selected from the group  
consisting of Cl, Br, and I; m is 1 or 2; and Ar is  
selected from the group consisting of:

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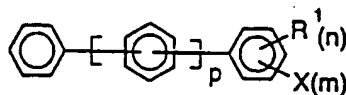
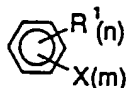


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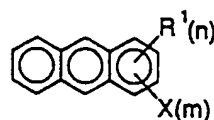
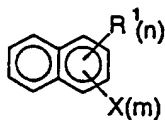


The aryl halide will have the general formulae:

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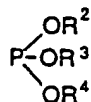
wherein  $p$  is 0 - 100, and  $R^1$  is independently alkyl, alkene, aryl, alkoxy, aryloxy, amine, amide, fluoroalkyl, fluoroaryl, ketone, ester, formyl, cyano, fluoro, imide, sulfone, thioether, and the like.  $X$  and  $R^1$  can be on any of the fused or multiple rings, and one to three CH units in any aromatic ring of each such Ar group can be replaced by a nitrogen atom. Any hydrogens of the aryl group may be substituted by  $R^1$  substituents; therefore,  $n$  is 0-5 for phenyl, 0-7 for naphthyl, 0-9 for anthracenyl, 0-9 for biphenyl, and so on. Furthermore, where  $m = 2$ , the two halides are at positions on the Ar group other than ortho to each other.

Other aryl halides that can be coupled in accordance with practice of the present invention will be apparent to one skilled in the art, including but not limited to binaphthyl halides, phenylnaphthyl halides, phenanthryl



1 halides, branched aryl halides, such as triphenylbenzene  
halides, and the like. Additionally, the aryl halides may  
be heteroaryl halides, wherein each ring of the aryl group  
may have one to three nitrogen atoms. Non-limited  
5 examples of heteroaryl halides are 2-chloropyridine,  
3-chloropyridine, 4-chloropyridine, haloquinolines,  
including the mono- and di-chloroquinolines,  
haloquinazolines, haloquinoxalines, halopyrazines, and the  
like.

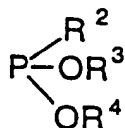
10 In one embodiment of practice of the present  
invention, the phosphite ligand has the formula:



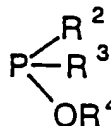
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wherein  $R^2$ ,  $R^3$ , and  $R^4$  are independently selected from the  
groups consisting of  $C_1$  to  $C_{22}$  alkyl,  $C_6$  to  $C_{24}$  aryl,  
alkaryl, and aralkyl.

20 In another preferred embodiment of practice of the  
present invention of coupling aryl halides to form biaryl  
or polyaryl compounds, the aryl halide is contacted in an  
anhydrous aprotic solvent with a catalyst mixture  
comprising a nickel compound, a reducing metal and a  
25 ligand selected from the group consisting of:



and



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wherein  $R^2$ ,  $R^3$ , and  $R^4$  are as defined above, to thereby  
form said biaryl or polyaryl compound.

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1           In yet another preferred embodiment of the present  
invention, a mixture comprising an aryl halide, a nickel  
compound or complex, and a phosphite ligand is prepared in  
an anhydrous aprotic solvent containing an electrolyte.  
5       The mixture is placed in an electrochemical cell  
comprising a cathode, and the aryl halide is cathodically  
reduced to form the biaryl or polyaryl compound.

          The present invention also defines a catalyst  
composition useful for aryl halide or aryl sulfonate  
10       coupling reactions. The composition includes a nickel  
compound or complex, a phosphite ligand, and a reducing  
metal selected from the group consisting of aluminum,  
magnesium, and zinc, and an optional promoter selected  
from chloride, bromide and iodide salts, wherein the molar  
15       ratio of ligand to nickel is between 1 and 10, and the  
molar ratio of reducing metal to nickel is between 1 and  
10,000.

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1     Detailed Description:

          This invention provides an efficient and economical method for coupling aryl halides or aryl sulfonates to form biaryl or polyaryl compounds. The method includes the steps of (1) providing an aryl sulfonate non-limiting examples of which include an aryl methanesulfonate (aryl mesylate), an aryl trifluoromethanesulfonate (aryl triflate), an aryl phenylsulfonate, an aryl tolylsulfonate (aryl tosylate), and an aryl fluorophenylsulfonate; or an aryl halide selected from the group consisting of an aryl chloride, an aryl bromide, and an aryl iodide, (2) contacting the aryl sulfonate or the aryl halide in an anhydrous aprotic solvent with a catalyst mixture comprising a nickel compound or complex, a phosphite ligand, an optional promoter selected from salts of chloride, bromide and iodide, and a reducing metal to thereby form the biaryl or polyaryl compound.

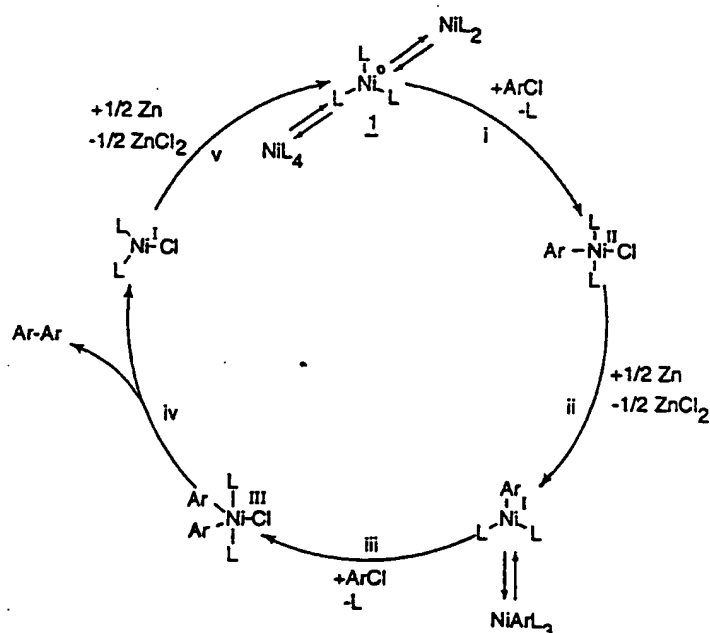
          As used herein, the term "aryl halide" includes aryl groups with a single halide substituent, as well as those which include two halide substituents. When the aryl halide has one halide substituent, a biaryl compound is formed. When the aryl halide has two halide substituents, a polyaryl compound is formed.

          Similarly, the term "aryl sulfonate" includes aryl groups with one or two sulfonate substituents. When the aryl sulfonate has one sulfonate substituent, a biaryl compound is formed. When the aryl sulfonate has two sulfonate substituents, a polyaryl compound is formed.

          A key to the development of the process of the present invention was the surprising discovery that complexes of phosphites and nickel catalyze the reductive coupling of aryl halides. It was also surprisingly found (1) that the concentration of the phosphite ligand

required to effectuate the aryl halide reactions is lower than the concentration of phosphine ligand when triarylphosphine catalyst systems are used, and (2) that constituent groups are not abstracted from the phosphite moiety into the aryl chloride substrate, as is the case with phosphine catalyst systems. Thus, the use of phosphite catalyst systems is more economical and results in less undesirable by-product than is the case when phosphine systems are used.

While not wishing to be bound by theory, the following catalytic cycle, where L is phosphite, is consistent with the known behavior of the catalyst systems of the present invention.



In the presence of the phosphite ligand L, the nickel salt, compound or complex that is added initially is

1 reduced to a Ni(0) phosphite complex 1. The Complex 1  
(the  $NiL_3$ ) species is in equilibrium with the  $NiL_4$  and  $NiL_2$   
species as shown. In step i, complex 1 oxidatively adds  
aryl halide to give a Ni(II) aryl complex. In step ii,  
5 the Ni(II) aryl complex is reduced by Zn (or other  
reducing agent) to give a Ni(I) complex which oxidatively  
adds a second aryl halide in step iii. Although it is not  
always shown explicitly, each Ni species in the cycle may  
add or lose ligand. Product biaryl is formed in step iv  
10 by reductive elimination to give a Ni(I) species which is  
reduced again to 1 in step v.

It is thought that the differing behaviors of the  
phosphine and phosphite ligands are probably related to  
the stability and reactivity of the Ni complexes.  
15 Phosphites are stronger pi acids than phosphines and give  
more stable complexes with low valent metals, such as  
nickel(0) but less stable complexes with higher valent  
metals, such as nickel(II). For example, it is known that  
tetrakis(triphenylphosphite) nickel(0) is very  
20 stable. For nickel(II) the complex  
bis(triphenylphosphine)nickel(II)chloride is stable and  
isolable, but the corresponding triphenylphosphite  
nickel(II) complex is not.

In one preferred embodiment, phosphites useful in  
25 conducting the coupling reaction of the present invention  
have the general structural formula:

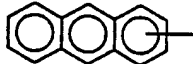


1 wherein  $R^2$ ,  $R^3$ , and  $R^4$  are independently selected from the group consisting of  $C_3$  to  $C_{22}$  alkyl,  $C_6$  to  $C_{24}$  aryl, alkaryl, and aralkyl.

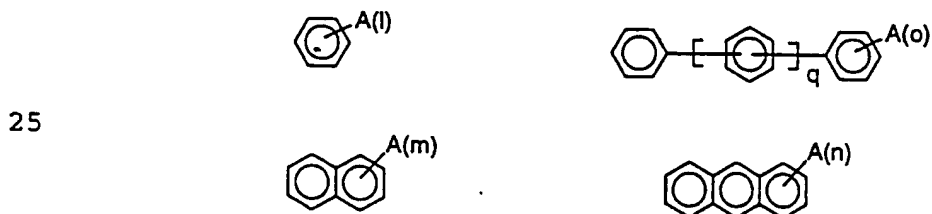
5 In the definition of  $C_6$  -  $C_{24}$  aryl groups, the number of carbons (C) refers to the carbons in the ring structure itself. For example,

10  is a  $C_6$  aryl;

 is a  $C_{10}$  aryl; and

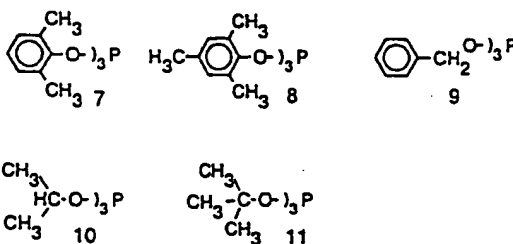
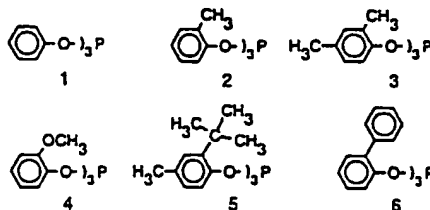
15  is a  $C_{14}$  aryl.

20 Non-limiting examples of aryl groups  $R^2$ ,  $R^3$ , and  $R^4$  useful in the phosphite ligands of the present invention are as follows:



30 wherein A is independently selected from the group consisting of  $C_1$  -  $C_{22}$  alkyl,  $C_6$  -  $C_{18}$  aryl,  $C_1$  -  $C_{12}$  alkoxy,  $C_6$  -  $C_{18}$  aryloxy, and F, and wherein  $l = 0-5$ ,  $m = 0-7$ ,  $n = 0-9$ , and  $o = 0-21$ ; the A groups can be on any of the fused or multiple rings; and  $q = 0-3$ .

Preferred embodiments of phosphite ligands useful in practice of the process of the present invention include the following:



The phosphites having the structures shown above are known compounds, and in general the phosphites required for the catalysts of the present invention are readily synthesized by those skilled in the art from simple starting materials.

The size of the R groups on the phosphite ( $P(OR)_3$ ) is an important consideration. If R is too small, e.g., methyl or ethyl, the Ni(O) complex will be too stable, and the catalyst will not be effective. Small R groups also favor dimeric Ni(O) and Ni(I) species which may not be catalytically active.

Additional phosphites with appropriate geometry useful in accordance with the present invention can be

1 deduced using the rules of cone angles known in the art.  
Using the methods of Tolman et al to calculate cone  
angles, catalysts comprising phosphites having cone angles  
between about 120° and 185° will be effective catalysts.  
5 Preferably, the phosphite will have a cone angle between  
about 125° and 170°, more preferably between about 130°  
and 160°, and most preferably between about 135° and 150°.  
Tri-2-tolylphosphite, a preferred phosphite, has a cone  
angle of 141°. The Tolman et al paper is incorporated  
10 herein by this reference.

A phosphite may be tested for its coupling activity  
using the following protocol. Coupling reactions of  
4-chlorotolulene are run using the general conditions set  
forth in Example 7 below, except that the amount of  
15 phosphite is adjusted to give phosphite to nickel (L/Ni)  
molar ratios of 2.01, 2.5, 3, and 4, and an internal  
standard such as biphenyl is added at the beginning of the  
reaction. The gas chromatograph (GC) yield of product  
dimethylbiphenyl is measured at 1, 2, 4, and 16 hours.  
20 Catalysts that give yields higher than approximately 10%  
for at least one combination of the L/Ni molar ratio and  
time are considered active. The dimethylbiphenyl yield  
should be 10%, preferably 20%, more preferably 50%, and  
most preferably at least 70%. Further experiments in  
25 which the temperature (in steps of about 10 to 20°C), the  
substrate to nickel ratio molar ratio (in increments of  
about 25 to 50%), and the nickel concentration (in  
increments of about 20 to 40%) are varied can be used to  
optimize the time and yield of the reaction. These  
30 conditions may also need to be modified when the same  
phosphite ligand is used in coupling different substrates.

The aryl halides which may be coupled using methods  
of the present invention include aryl chlorides, aryl

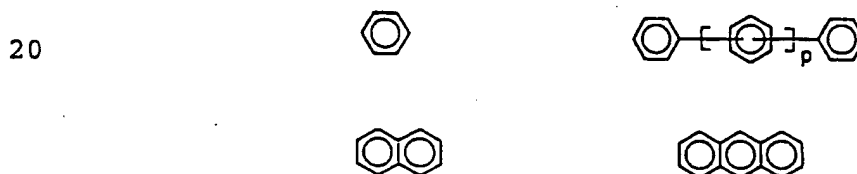


1 bromides, and aryl iodides. It was discovered that aryl  
fluorides are not reactive under the conditions of the  
process of the present invention. Aryl chlorides are  
5 preferred because they typically result in less side  
product produced by reductive replacement of the halide  
group with hydrogen. Additionally, aryl chlorides are  
usually less costly than aryl bromides or aryl iodides.  
Preferably, the aryl group does not bear substituents  
10 which react with the nickel catalyst or with the reductive  
metal. Such groups include nitro groups, free acid  
groups, or protic groups such as alcohol.

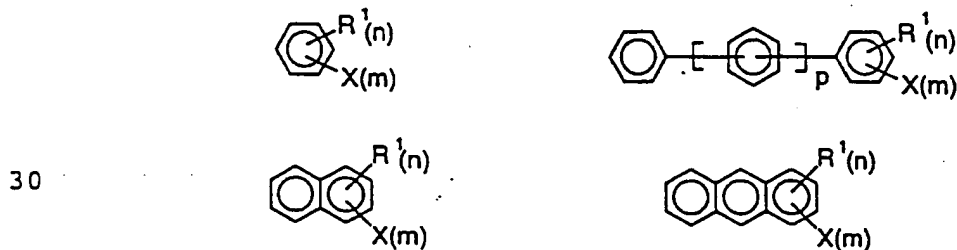
In a preferred embodiment, aryl halides which may be  
coupled using the methods of the present invention have  
the following general formula:



wherein X is independently selected from the group  
consisting of Br, Cl, I, m is 1 or 2, n is 0-10, and p is  
0-100; Ar is selected from the group consisting of:



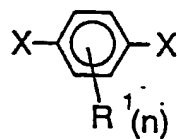
25 to provide aryl halides having the general structures:



1 wherein p is 0 - 100; R<sup>1</sup> is independently alkyl, alkene,  
 aryl, alkaryl, aralkyl, aryloxy, amine, amide (-NR'COR" or  
 5 -CONR'R"), fluoroalkyl, fluoroaryl, ketone (including  
 alkyl ketone and aryl ketone), ester (-CO<sub>2</sub>R' or -OCOR'),  
 formyl (-COH), cyano (-CN), fluoro, imide, sulfone  
 (-SO<sub>2</sub>R), and thioether (R' and R" are alkyl or aryl);  
 wherein X and R<sup>1</sup> can be on any of the fused or multiple  
 rings; wherein one to three CH units in any aromatic ring  
 10 of each such Ar group can be replaced by a nitrogen atom,  
 and where m = 2, the two halides are at positions other  
 than ortho to each other.

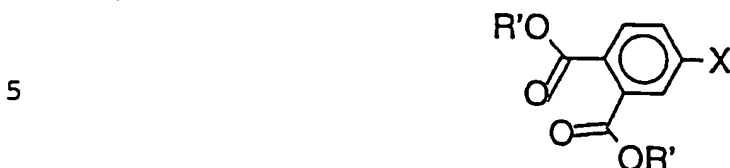
The aryl halides useful for coupling using the nickel  
 phosphite catalysts of the present invention are either  
 15 commercially available or readily synthesized by those  
 skilled in the art. For example, chlorobenzoates,  
 bromobenzoates, 2,3 and 4-chloroacetophenone, 2,3 and  
 4-chlorobenzophenone, 2,3 and 4-chlorobenzonitrile,  
 2,4-dichlorofluorobenzene, 2,5-dichlorotoluene, and the  
 like are commercially available. Preparation of aryl  
 20 chlorides and aryl dichlorides having ketone substituents  
 may be accomplished by Friedel-Crafts acylation, as for  
 example in U.S. Patent No. 5,210,313, issued May 11, 1993,  
 which discloses preparation of dichlorobenzophenones.

In one embodiment, the aryl halide has the formula:



30 wherein X and R<sup>1</sup> are as defined above.

1 In another embodiment, the aryl halide has the  
formula:



10 wherein X is as defined above and R' is alkyl or aryl.

In practice of the present invention, to form polyaryl compounds, aryl monohalides may be added to one or more aryl dihalides. The aryl monohalides act as endcappers and control the molecular weight of the polyaryl compound (the polymer) formed.

Non-limiting examples of R' groups are as follows:

alkyl groups are methyl, ethyl, propyl, isopropyl, tert-butyl, cyclohexyl, stearyl, and docosyl (-CH<sub>2</sub>(CH<sub>2</sub>)<sub>20</sub>CH<sub>3</sub>);

20 aryl groups are phenyl, biphenyl, naphthyl, anthracenyl, and diphenylphenyl;

alkaryl groups are o-tolyl, p-tolyl, m-tolyl, t-butylphenyl, dinonylphenyl, and poly(dioctylphenylene);

25 aryalkyl groups are phenyloctyl and naphthylmethyl;

C bound amides are N,N-dimethylaminocarbonyl (-CON(CH<sub>3</sub>)<sub>2</sub>), N,N-diphenylaminocarbonyl, piperidinecarbonyl (-CONCH<sub>2</sub>CH<sub>2</sub>CH<sub>2</sub>CH<sub>2</sub>CH<sub>2</sub>), morpholinecarbonyl (-CONCH<sub>2</sub>CH<sub>2</sub>OCH<sub>2</sub>CH<sub>2</sub>), and N-methyl-N-phenylaminocarbonyl;

30 N bound amides are benzoylamino, N-methylacetylamino;

O bound esters are acetyloxy (-OCOCH<sub>3</sub>) and benzoyloxy (-OCOC<sub>6</sub>H<sub>5</sub>);

1 C bound esters are methoxycarbonyl ( $-\text{CO}_2\text{CH}_3$ ) and  
phenoxycarbonyl ( $-\text{CO}_2\text{C}_6\text{H}_5$ );  
alkoxy groups are methoxy, neopentyloxy, and  
cyclohexyloxy;  
5 aryloxy groups are phenoxy, naphthoxy, and  
biphenyloxy;  
alkene groups are groups that include a double  
bond between two carbons of the group, for example vinyl,  
and propenyl;  
10 ketones are phenylketone (also called benzoyl),  
naphthylketone (naphthoyl), methylketone (acetyl),  
ethylketone (propionyl), tert-butylketone (pivaloyl),  
isobutylketone, trifluoromethylketone (trifluoroacetyl),  
methoxyethylketone, benzylketone, phenethylketone, 2,4,6-  
15 trimethylphenylketone, pyridinylketone (nicotinoyl),  
2-quinolinoketone, and 2-thiopheneylketone;  
imides are phthalimide, fluorophthalimide, and  
succinimide;  
fluoroaryl groups are fluorophenyl and  
20 perfluorophenyl; and  
fluoroalkyl groups are trifluoromethyl,  
perfluoro butyl, and 2,2,2-trifluoroethyl.  
In the reaction of the present invention, it is  
typically sufficient to maintain the phosphite ligand to  
25 nickel molar ratio in the range of about 2 to 10;  
preferably in the range of about 2.4 to 5; more preferably  
in the range of about 2.5 to 3.5; and most preferably in  
the range of about 2.8 to 3.2. It appears that the  
optimum ligand to nickel ratio is about 3. The useful  
30 range of ligand to nickel ratio depends on the size of the  
phosphite ligand. For small phosphites, such as  
triphenylphosphite, the nickel (0) tetrakisphosphite  
complex ( $\text{NiL}_4$ ) is very stable, so that the phosphite to

1 nickel ratio must be kept below about 4. For larger  
phosphites, such as tri-2-tolylphosphite, the  $NiL_4$  complex  
is destabilized, and larger amounts of phosphite may be  
used; for example, up to 25 M equivalents of phosphite  
5 relative to nickel or higher may be used, although at  
these high levels, the reaction rate becomes slower.

In the systems of the present invention the amount of  
phosphite relative to nickel is substantially less than  
the concentration of phosphine to nickel in nickel  
10 phosphine catalyst systems. For example, while in the  
present systems the molar ratio of phosphite to nickel is  
less than 10 and often may be less than 4 or 5, the molar  
ratio of phosphine to nickel in nickel phosphine systems  
is usually 5 to 10 equivalents and excess phosphine  
15 improves yields.

It has been found that when using nickel/phosphite  
catalysts, the phosphite ligand concentration can be kept  
much lower than the phosphine ligand concentration when  
nickel/phosphine catalyst systems are used. Additionally,  
20 it has been found that the abstraction of aryl groups from  
the phosphite ligand is completely precluded. This  
reduces side reactions and resultant formation of  
contaminating by-products that result from abstraction of  
aryl groups when nickel phosphine catalyst systems are  
25 used. Apparently, nickel does not insert into the  
phosphite's O-aryl or P-O bonds as it does into P-aryl  
bonds of phosphines. It is this insertion of nickel (O)  
into the P-aryl bonds of phosphines, as has been described  
by D.R. Fahey and J.E. Mahan (*J. Am. Chem. Soc.*, 98, 449  
30 (1976)), which is a source of by-products in the  
nickel/phosphine catalyst systems.

An additional advantage of phosphite ligands is  
manifest during the work-up of the catalytic coupling

1 product. Since alkyl and aryl phosphites are easily  
hydrolyzed and/or oxidized to water soluble phosphites and  
phosphates the product is readily cleansed of phosphite  
ligand by treatment with aqueous base. A similar process  
5 is not possible with phosphines which do not hydrolyze so  
easily.

In practice of this present invention, the nickel may  
be introduced into the reaction mixture in any form which  
can be reduced by the reducing agent to give a nickel(0)  
10 phosphite complex. Zero valent nickel/ligand complexes  
are also useful as long as the ligands are weak enough to  
be displaced by the phosphite ligands. Non-limiting  
examples of sources of nickel include nickel (II)  
chloride, bromide, iodide, acetate, acetoacetate,  
15 carbonate, sulfate, formate, toluene sulfonate, and  
similar salts. Nickel complexes such as  
bistriphenylphosphine nickel (II) chloride or  
trisbipyridyl nickel (II) may be used. Nickel compounds  
and complexes in the zero valent state may also be used  
20 including nickel (0) biscyclooctadiene,  
tetrakis(triphenylphosphine) nickel (0), nickel (0)  
ethylene tris(triarylphosphite), and the like. Most  
labile nickel compounds, i.e., nickel compounds where the  
Ni is free to exchange a ligand, may be used. Counter  
25 ions are not critical but should not be oxidants, such as  
nitrate, or react with low valent nickel or the reducing  
agent. The nickel compound will exchange its original  
ligands or anions for phosphite ligands to form soluble  
nickel phosphite complexes. The formation of the nickel  
30 phosphite complexes may require the presence of the  
reducing agent. Nickel compounds which bind nickel too  
tightly, such as nickel tetraphenylporphyrin, are not

1 effective. Nickel (I) compounds, although rare, may also  
be used.

Suitable reducing metals for use in practice of the  
present invention are aluminum, manganese, zinc, and  
5 alkaline earths such as calcium and magnesium. The metal  
should be finely divided powders or dust, preferably with  
a particle size less than about 100 mesh, and more  
preferably with a particle size less than about 150 mesh.  
The metal powder should be activated by treatment with  
10 acid, followed by washing and drying. For example, highly  
active zinc powder is made by treating zinc dust (-350  
mesh) with HCl in diethylether, washing, drying and  
resieveing (if necessary) to -150 mesh, where the minus  
sign (-) indicates that all powder which goes through the  
15 sieve is taken. Activated metals must be protected from  
air before use. Zinc powder activated using the procedure  
outlined in Example 1 set forth below is preferred.

Some reduction of substrate (i.e., replacement of  
halide by hydrogen) also occurs by way of nickel  
20 catalysis. Any water or protic solvent present, such as  
alcohols or acids, will lead to reduction. Even in  
anhydrous aprotic solvents, reduction may occur,  
especially with substrates which are slow to react,  
typically those containing electron donating groups like  
25 alkoxy and alkyl placed ortho or para to the halide.

It may not be possible to eliminate such reduction,  
and some minimum level of reduction of the substrate may  
have to be tolerated. In general, it has been found that  
catalysts with higher rates of product formation give less  
30 reduction. It is the relative rates of coupling and  
reduction that determine the product composition.

In another embodiment of practice of the present  
invention, the reducing equivalents may be supplied

1 cathodically instead of by a reducing metal. The cathode  
should be an inert metal such as platinum or steel, or an  
inert non-metal conductor such as graphite. The solvent  
5 must contain an electrolyte, such as an alkali or alkaline  
earth halide, zinc halide, or alkylammonium halide. Most  
common electrolytes are acceptable, including but not  
limited to, alkali metal and alkaline earth metal salts,  
alkyl ammonium halides, and zinc halides. The electrolyte  
10 should be at least 0.01 M, preferably 0.1 M, and more  
preferably 1 M in concentration. The anode may be an  
inert metal or conductor such as platinum or carbon  
respectively, or a sacrificial anode such as zinc or tin.  
The appropriate range of applied potential or controlled  
15 current will be apparent to one skilled in the art. In  
general, the current will be controlled from about 10  
ma/cm<sup>2</sup> to about 2 A/cm<sup>2</sup>, preferably between about 100  
ma/cm<sup>2</sup> to 1 A/cm<sup>2</sup>, and more preferably between about 200  
ma/cm<sup>2</sup> to about 600 ma/cm<sup>2</sup>.

20 A divided cell is not necessary; however, anodic  
products are more easily separated in a divided cell.  
Where it is advantageous to avoid contamination of the  
product by the oxidized form of the reducing agent,  
electrochemical coupling in a divided cell is the method  
of choice. The usual principles of electrochemistry  
25 apply. Electrochemical techniques are generally preferred  
at small scale production. In some cases, electrochemical  
methods give better control over by-product formation  
since reduction potentials may be set to values not  
available with chemical reducing agents.

30 Preferably, a promoter is included in the catalyst  
system of the present invention. Useful promoters are  
chloride, bromide and iodide ions. The promoter ions may  
be introduced as alkali or alkaline earth salts,



1 alkylammonium salts, or aluminum, manganese or zinc salts.  
Bromide and iodide salts are preferred. The amount of  
promoter may range from 0.01 M to 1 M, preferably from 0.1  
5 M to 0.5M, and most preferably from 0.2M to 0.4M. Other  
promoters useful in practice of the present invention  
include sulfate, sulfonate, phosphate, and phosphonate  
salts of alkali or alkaline earth metals,  $Al^{+++}$ ,  $Mn^{++}$ ,  $Zn^{++}$ ,  
or alkyl ammonium. Bidentate aromatic heterocyclic  
10 ligands such as bipyridyl, phenanthroline, and the like  
can also be used as promoters.

The reaction solvents should be aprotic and must  
dissolve the nickel phosphite catalyst to at least 0.0001  
M in nickel, preferably to at least 0.001 M in nickel, and  
most preferably to at least 0.01 M in nickel. Polar  
15 solvents are preferred, including but not limited to  
dimethylsulfoxide (DMSO), sulfolane, N-methylpyrrolidinone  
(NMP), N,N-dimethylacetamide (DMAC),  
N-cyclohexylpyrrolidinone, dimethylformamide (DMF),  
N,N,N,N-tetramethylurea, and the like. These solvents can  
20 be mixed with other aprotic solvents such as benzene,  
butyrolactone, cyclohexane, diglyme, heptane,  
propylenecarbonate, tetrahydrofuran, toluene, xylenes, and  
other saturated aliphatic hydrocarbons, aromatic  
hydrocarbons, or ethers.

25 The solvents useful in accordance with the present  
invention are preferably anhydrous. The presence of water  
leads to reductive replacement of the halide group with  
hydrogen, and to deactivation of the catalyst. The  
concentration of water should be kept below 1000 ppm,  
30 preferably below 500 ppm, more preferably below 100 ppm,  
and most preferably below 50 ppm. The concentration of  
water may be reduced further to 40 ppm, 30 ppm, or even 20  
ppm or 10 ppm, to avoid possible side reactions involving

1        water. Water may be reduced to these levels, for example,  
by addition of activated molecular sieves, or by other  
methods known in the art.

5        The reaction temperature for coupling should  
typically be from about 0°C to about 120°C. The  
temperature may be adjusted to optimize the product yield,  
for example, temperatures of 50°C, 70°C, 90°C, or 100°C  
may be preferred for a particular substrate.

10       The reaction pressure is not critical. Either  
elevated or reduced pressure may be used as required. The  
reaction must be carried out under inert atmosphere,  
typically nitrogen. Other inert gases such as helium,  
argon, and the like may also be used.

15       Reaction time is dependent on temperature,  
concentration of catalyst and reactants, and amount of  
promoter. Reaction time is typically between 2 and 24  
hours. There is usually no maximum reaction time since  
the product is usually inert to the catalyst.

20       The following examples are illustrative of the  
present invention but are not considered limiting thereof  
in any way.

#### EXAMPLE 1

##### 25       Preparation of Activated Zinc Dust

Activated zinc dust is obtained after 2 washings of  
commercially available 325 mesh zinc dust with 1 M  
hydrogen chloride in diethyl ether (anhydrous) followed by  
2 washings with diethyl ether (anhydrous) and drying in  
30       vacuo or under inert atmosphere for several hours at about  
100-200°C. If clumps form during drying the zinc dust is  
re-sieved to -150 mesh. This material should be used

1 immediately or stored under an inert atmosphere away from  
oxygen and moisture.

#### EXAMPLE 2

5 Coupling of N-(4-Chloro-2-benzoylphenyl)succinimide  
using a nickel catalyst comprising  
tri(2-methylphenyl) phosphite

A solution of anhydrous nickel chloride (49 mg,  
0.38 mmol), sodium iodide (300 mg, 2 mmol), tri(2-  
methylphenyl) phosphite (370 mg, 1.05 mmol) and N-(4-  
10 chloro-2-benzoylphenyl) succinimide (2.79 g, 8.9 mmol) in  
NMP (7 ml) was prepared in a glovebox and then stirred at  
60°C for 3 hours. Activated zinc dust (1.6 g, 24.6 mmol)  
prepared in accordance with the procedure of Example 1 was  
added to the homogeneous green solution under helium. The  
15 mixture was stirred at 60°C for 13 hours at 80°C for  
another 6 hours. The reaction mixture was poured into  
50 ml of water and filtered. The solid was collected by  
filtration and then stirred in 20 ml of methanol for 2  
hours. The suspension was filtered and the cake was  
20 washed in the funnel with methylene chloride. Most of the  
solid dissolved and the solvent in the filtrate was  
evaporated. The solid was stirred in methanol and  
filtered to give pure coupling product as crystals. The  
crystals were air-dried to give 2.02 g 3,3'-dibenzoyl-  
25 4,4'-succinimidobiphenyl (82%).

#### EXAMPLE 3

Coupling Reaction of 4-Chlorotoluene using a nickel  
catalyst comprising tri(2-methylphenyl) phosphite

30 A mixture of anhydrous nickel chloride (50 mg,  
0.39 mmol), sodium iodide (300 mg, 2 mmol), tri(2-  
methylphenyl)phosphite (300 mg, 0.85 mmol) in NMP (5 ml)

1 was prepared in a glovebox and then stirred at 60°C for 1  
hour 50 minutes. To the resulting green solution was  
added activated zinc dust (1.5 g, 23 mmol) prepared in  
accordance with the procedure of Example 1 under helium.  
5 The mixture was stirred at 60°C and 4-chlorotoluene (1 g,  
7.9 mmol) was added. After 17 hours, the reaction  
temperature was raised to 80°C and the mixture was stirred  
for another 7 hours. 4,4'-dimethylbiphenyl was obtained  
in 97% yield by gas chromatography analysis of the  
10 reaction mixture. The GC retention time of the dimer was  
the same as that of dimer obtained using a literature  
coupling method.

#### EXAMPLE 4

15 **Coupling Reaction of 2-Chlorobenzophenone using a nickel  
catalyst comprising tri(2-methylphenyl) phosphite**

A mixture of anhydrous nickel chloride (50 mg,  
0.39 mmol), sodium iodide (300 mg, 2 mmol), tri(2-  
methylphenyl)phosphite (340 mg, 0.97 mmol),  
20 2-chlorobenzophenone (1.01 g, 4.7 mmol) and zinc chloride  
(1g, 7.4 mmol) in NMP (8 ml) was prepared in a glovebox  
and then stirred at 60°C for 1 hour. To the solution was  
added activated zinc dust (1.5 g, 23 mmol) prepared in  
accordance with the procedure of Example 1 under helium.  
25 The mixture was stirred at 60°C for 13 hours.  
2,2'-dibenzoylbiphenyl was obtained quantitatively based  
on GC analysis. The GC retention time of the dimer was  
the same as that of dimer obtained using a literature  
coupling method.

30

1

EXAMPLE 5

Coupling of 2-Chlorobenzophenone using a nickel catalyst comprising triphenyl phosphite

5 A solution of anhydrous nickel chloride (50 mg, 0.39 mmol), sodium iodide (300 mg, 2 mmol), triphenylphosphite (250 mg, 0.81 mmol), 2-chlorobenzophenone (1.01 g, 4.7 mmol) in NMP (5 ml) was prepared in a glovebox and then stirred at 70°C for 2 hours. To the solution was added activated zinc dust (1.6 g, 25 mmol) prepared in accordance with the procedure of Example 1 under helium. It was stirred at 70°C for 13 hours. 2,2'-Dibenzoylbiphenyl was obtained in 96% yield based on GC analysis. The GC retention time of the dimer was the same as that of dimer obtained using a literature coupling method.

15

EXAMPLE 6

Polymerization of 2,5-Dichlorobenzophenone Using A Nickel Catalyst Comprising Tri(2-methylphenyl)phosphite

20 A solution of anhydrous nickel chloride (47 mg, 0.36 mmol), sodium iodide (150 mg, 1 mmol), tri(2-methylphenyl)phosphite (700 mg, 1.99 mmol) and 2,5-dichlorobenzophenone (1.2 g, 4.8 mmol) in NMP (5 ml) was prepared in a glovebox and then stirred at 90° C for 40 minutes. Activated zinc dust (1.5 g, 23 mmol) prepared in accordance with the procedure of Example 1 was added to the homogeneous green solution under helium. The mixture was stirred at 90° C for 36 hours and then cooled to room temperature. The viscous solution was poured into 1 M HCl in ethanol. The solid was collected by filtration and was stirred in acetone for further purification. The polymer was obtained in 92% yield (0.79 g) after filtration and drying. Size exclusion chromatography (SEC) of the

30

35

1 polymers relative to narrow polydispersity polystyrene  
standards, for dilute solutions of the polymer in NMP  
including 0.05 molar lithium bromide, indicated a weight  
average molecular weight of 14,319.

5

#### EXAMPLE 7

##### Coupling of 4-Chlorotoluene using a nickel catalyst comprising Tri(2-phenylphenyl)phosphite

A solution of nickel chloride (50 mg, 0.39 mmol),  
10 sodium iodide (300 mg, 2 mmol), tri(2-  
phenylphenyl)phosphite (524 mg, 0.97 mmol) and 4-  
chlorotoluene (1 g, 7.9 mmol) in NMP (5 ml) was prepared  
in a glovebox and then stirred at 70°C for 2 hours.  
Activated zinc dust (1.6 g, 25 mmol) prepared in  
15 accordance with the procedure of Example 1 was added to  
the solution under helium. The mixture was stirred at  
60°C for 13 hours. Dimethylbiphenyl was obtained in 99%  
yield based on GC analysis. The GC retention time of the  
dimer was the same as that of dimer obtained using a  
20 literature coupling method.

#### EXAMPLE 8

##### Coupling of 2-Chlorobenzophenone using a nickel catalyst comprising tri(2-phenylphenyl) phosphite

25 A solution of anhydrous nickel chloride (25 mg,  
0.19 mmol), sodium iodide (60 mg, 0.39 mmol), tri(2-  
phenylphenyl)phosphite (262 mg, 0.49 mmol),  
2-chlorobenzophenone (2 g, 9.3 mmol) in NMP (5 ml) was  
prepared in a glovebox and then stirred at 60°C for 2  
30 hour. To the solution was added activated zinc dust  
(0.75 g, 11.7 mmol) prepared in accordance with the  
procedure of Example 1 under helium. It was stirred at  
60°C for 11 hours. 2,2'-Dibenzoylbiphenyl was obtained in

1        99% yield based on GC analysis. The GC retention time of  
the dimer was the same as that of dimer obtained using a  
literature coupling method.

5

EXAMPLE 9

Coupling of 3-Chlorobenzophenone using a nickel catalyst  
comprising tri(2-phenylphenyl) phosphite

A solution of anhydrous nickel chloride (50 mg,  
0.39 mmol), sodium iodide (300 mg, 2 mmol), tri(2-  
10 phenylphenyl)phosphite (524 mg, 0.98 mmol), 3-  
chlorobenzophenone (2 g, 9.3 mmol) in NMP (5 ml) was  
prepared in a glovebox and then stirred at 60°C for 2  
hours. To the solution was added activated zinc dust  
(1.4 g, 21.5 mmol) prepared in accordance with the  
15 procedure of Example 1 under helium. It was stirred at  
60°C for 4 hours. 3,3'-dibenzoylbiphenyl was obtained in  
97% yield based on GC analysis. The GC retention time of  
the dimer was the same as that of dimer obtained using a  
literature coupling method.

20

EXAMPLE 10

Coupling of 4-Chlorotoluene using a nickel catalyst  
comprising Tri(2-methoxyphenyl)phosphite

A solution of nickel chloride (50 mg, 0.39 mmol),  
25 sodium iodide (300 mg, 2 mmol), and tri(2-  
methoxyphenyl)phosphite (360 mg, 0.9 mmol) in NMP (5 ml)  
was prepared in a glovebox and then stirred at 60°C for  
1.5 hours. Activated zinc dust (1.6 g, 25 mmol) prepared  
in accordance with the procedure of Example 1 was added to  
30 the solution under helium followed by 4-chlorotoluene  
(1 g, 7.9 mmol). The mixture was stirred at 60°C for 30  
hours and at 80°C for another 15 hours. Dimethylbiphenyl  
was obtained in 99% yield based on GC analysis. The GC

35

1 retention time of the dimer was the same as that of dimer  
obtained using a literature coupling method.

#### EXAMPLE 11

5 Coupling of 2-Chlorobenzophenone using a nickel catalyst  
comprising tri(2-methylphenyl) phosphite

A solution of anhydrous nickel chloride (50 mg,  
0.39 mmol), sodium iodide (300 mg, 2 mmol), tri(2-  
methoxyphenyl)phosphite (360 mg, 0.9 mmol), 2-  
10 chlorobenzophenone (1.2 g, 5.6 mmol) in NMP (5 ml) was  
prepared in a glovebox and then stirred at 60°C for 2  
hour. To the solution was added activated zinc dust (1.4  
g, 21.5 mmol) prepared in accordance with the procedure of  
Example 1 under helium. It was stirred at 60°C for 12  
15 hours. 2,2'-Dibenzoylbiphenyl was obtained in 97% yield  
based on GC analysis. The GC retention time of the dimer  
was the same as that of dimer obtained using a literature  
coupling method.

20

#### EXAMPLE 12

Coupling of 4-Chlorotoluene using a nickel catalyst  
comprising Tri(2-tert-butylphenyl)phosphite

A solution of anhydrous nickel chloride (50 mg,  
0.39 mmol), sodium iodide (310 mg, 2.07 mmol), and tri(2-  
25 tert-butylphenyl)phosphite (508 mg, 0.97 mmol) in NMP (5  
ml) was prepared in a glovebox and then stirred at 60°C  
for 1.5 hours. Activated zinc dust (1.5 g, 23 mmol)  
prepared in accordance with the procedure of Example 1 was  
added to the solution under helium followed by 4-  
30 chlorotoluene (1g, 7.9 mmol). The mixture was stirred at  
60-65°C for 15 hours. Dimethylbiphenyl was obtained in  
99% yield based on GC analysis. The GC retention time of



1 the dimer was the same as that of dimer obtained using a  
literature coupling method.

#### EXAMPLE 13

5 Preparation of 6-chloro-2-(4-fluorophenyl)-4-  
phenylquinoline

A three-necked, 2 L round-bottomed flask equipped  
with a thermometer, a mechanical stirrer and a  
distillation unit fitted with a nitrogen inlet valve was  
10 charged with 2-amino-5-chlorobenzophenone (695.0 g, 3.00  
mol), and 4'-fluoroacetophenone (456.0 g, 3.30 mol),  
p-tosic acid (47.62 g, 0.25 mol). The reaction mixture  
was heated under nitrogen at 165°C (44 h). The yellow  
4'-acetophenone that co-distilled with the water was  
15 separated and reintroduced to the reaction mixture  
throughout the heating period. The mixture was further  
heated to 190°C (2 h). The mixture was cooled to 120°C  
and was poured into 95% ethanol (10 L) while vigorously  
stirring with a mechanical stirring rod set up. The  
20 mixture was filtered and the precipitate was washed with  
ethanol (1 L). The solid was dried in a vacuum oven at  
80°C (16 h). Yield 969 g, 97%; mp 141.0-142.1°C.

#### EXAMPLE 14

25 Preparation of 6,6'-bis[2-(4-fluorophenyl)-4-  
phenylquinoline]

A three-necked, 22 L round-bottomed flask equipped  
with a mechanical stirred, a thermometer, and a nitrogen  
inlet was charged with nickel chloride (27.38 g, 0.211  
30 mol), tris(2-tolyl)phosphite (230.7 g, 0.655 mol), sodium  
iodide (167.8 g, 1.12 mol), 6-chloro-2-(4-fluorophenyl)-4-  
phenylquinoline (1713 g, 5.13 mol), and NMP (4.32 L). The  
mixture was heated to 80°C under nitrogen (24 h). The

1 temperature of the reaction was lowered to 60°C and zinc  
(455.7 g, 6.97 mol) was added. The reaction exothermed to  
95°C, with the aid of a cooling bath for temperature  
control. The mixture was stirred again at 80°C (24 h).  
5 The mixture was heated further to 160°C until all of the  
solids had dissolved and was then filtered hot through  
Celite. The mother liquor was cooled to room temperature,  
the crude product was collected by filtration, and the  
crude product was washed with methanol (4 L). The solid  
10 was dissolved in DMF (20 L) and subjected to another hot  
filtration through Celite. The yellow crystals that  
formed in the DMF filtrate were collected by filtration  
and washed with methanol (2 L). The solid was dried in a  
vacuum oven at 120 °C (16 h). Yield 1147 g, 74.9%.

15

#### EXAMPLE 15

Preparation of 6,6'-bis[2-(4-fluorophenyl)-4-  
phenylquinoline] in a single pot from 2-amino-5-  
chlorobenzophenone and 4'-fluoroacetophenone

20

A 250 mL, three-necked, round-bottomed flask fitted  
with a mechanical stirring set-up, a short path  
distillation apparatus, and a nitrogen inlet valve was  
charged with 2-amino-5-chlorobenzophenone (Compound 3)  
25 (17.4 g, 75.0 mmol), 4'-fluoroacetophenone (Compound 2)  
(10.0 mL, 824 mmol), and tosic acid (0.505 g, 2.7 mmol).  
The reaction was heated under nitrogen at 180°C (20 h) to  
effect condensation and water removal. The temperature of  
the reaction was lowered to 160°C, and potassium carbonate  
30 (0.367 g, 2.7 mmol) was added. Toluene (100 mL) was then  
added to the reaction and distilled away. This toluene  
addition/distillation was repeated two times.

35

1           The temperature of the reaction was lowered to 80°C,  
and the distillation unit was removed. The flask was  
charged with nickel chloride (0.778 g, 6.00 mmol), sodium  
iodide (2.43 g, 16.2 mmol), tris(2-tolyl)phosphite (6.77  
5 g, 19.2 mmol), and NMP (63 mL), and the resulting solution  
was stirred (18 h). The reaction temperature was then  
lowered to 60°C, and activated zinc dust (6.59 g, 101  
mmol) was added. After the exotherm had subsided (10  
min), the reaction was allowed to stir at 80°C (16 h).

10           The temperature of the reaction was raised to 160°C  
to dissolve the precipitate which had formed. The  
reaction mixture was filtered while hot through Celite and  
was allowed to cool to room temperature. The crude  
product was collected by filtration and was washed with  
15 ethanol. A second crop was collected from the mother  
liquor and was washed with ethanol. The yellow product  
was dried in a vacuum oven at 160°C (18 h). 12.0 g from  
Crop 1 and 6.3 g from Crop 2 (Yield 73.1%).

          In a second embodiment aryl sulfonates are coupled to  
20 biaryls and aryl disulfonate are coupled to polyaryls  
using the same nickel phosphite catalyst and conditions as  
for aryl halides. Thus, anhydrous dipolar aprotic  
solvents such as NMP, DMF, and DMAC are suitable. The  
reducing agents may be reducing metals such as aluminum,  
25 calcium, magnesium, manganese, zinc and their alloys. The  
reaction temperatures are from 25°C to 150°C, preferably  
50°C to 100°C, and more preferably from 75°C to 90°C. The  
reaction times are from 1 to 72 hours, preferably from 2  
to 24 hours and more preferably from 4 to 16 hours. The  
30 phosphite ligand to nickel molar ratio should be from  
about 2:1 to about 4:1. The aryl halide to nickel ratio  
should be from about 10:1 to about 10,000:1, preferably  
from about 20:1 to about 1000:1, more preferably from

1        about 25:1 to 100:1, and most preferably from about 40:1  
to about 80:1.

5        The above descriptions of various embodiments of  
processes for coupling aryl halides or aryl sulfonates to  
produce biaryls or polyaryls and the catalyst compositions  
useful for such coupling reactions are provided for  
illustrative purposes. Because of variations which will  
be apparent to those skilled in the art, the present  
invention is not intended to be limited to the particular  
10        embodiments described above. Additionally, it should be  
understood that any compounds or compositions that are not  
described in the application as being useful for  
practicing the invention, are not needed and the invention  
can be practiced in their absence.

15        The scope of the invention is defined in the  
following claims.

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## 1      WHAT IS CLAIMED IS:

1.      A method of coupling aryl halides to form biaryl  
or polyaryl compounds, the method comprising the steps of:  
5            providing an aryl halide selected from the group  
consisting of an aryl chloride, an aryl bromide, and an  
aryl iodide; and

          contacting the aryl halide in an anhydrous  
aprotic solvent with a catalyst mixture comprising a  
10          nickel compound, a phosphite ligand, and a reducing metal  
to thereby form said biaryl or polyaryl compound.

2.      The method according to claim 1, wherein the  
catalyst mixture additionally comprises a promoter  
15          selected from the group consisting of chloride, bromide,  
and iodide salts.

3.      The method according to claim 2, wherein the  
promoter is sodium iodide.  
20

4.      The method according to claim 2, wherein the  
promoter is sodium bromide.

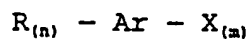
5.      The method according to claim 1, wherein the  
25          phosphite ligand to nickel molar ratio is in the range of  
2 to 10.

6.      The method according to claim 1, wherein the  
phosphite ligand to nickel molar ratio is in the range of  
30          2.4 to 5.

7.      The method according to claim 1, wherein the  
reducing metal is selected from the group consisting of

1 aluminum, calcium, magnesium, manganese, zinc, alloys of  
aluminum, calcium, magnesium, manganese, and zinc, and  
mixtures thereof.

5 8. The method according to claim 1, wherein the  
aryl halide has the formula:



wherein X is independently selected from the group  
consisting of Cl, Br, I, m is 1 or 2, and n is 0-10;

10 Ar is selected from the group consisting of:

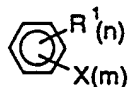


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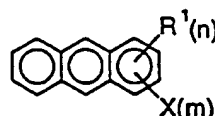
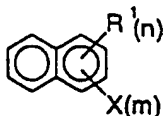


and the aryl halide has the formula:

20



25



wherein p is 0 - 100;

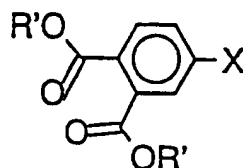
30 R is independently alkyl, alkene, aryl, alkoxy,  
aryloxy, amine, amide, fluoroalkyl, fluoroaryl, alkyl  
ketone, aryl ketone, ester, formyl, cyano, fluoro, imide,  
sulfone, and thioether;

35

1                    wherein X and R can be on any of the fused or  
multiple rings;

                  wherein one to three CH units in any aromatic  
ring of each such Ar group can be replaced by a nitrogen  
5                   atom, and where  $m = 2$ , the two halides are at positions  
other than ortho to each other.

                  9.    The method according to claim 1 wherein the aryl  
10                  halide is

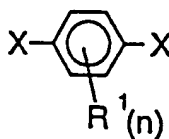


15                  wherein X is selected from the group consisting of Cl, Br,  
and I; and R' is alkyl or aryl.

                  10.   The method according to claim 1, wherein the  
20                  aryl halide includes two halide groups.

                  11.   The method according to claim 8, wherein the  
aryl halide includes two halide groups para to each other.

25                  12.   The method according to claim 1, wherein the  
aryl halide has the formula:

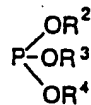


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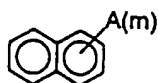
- 1 wherein X is independently selected from the group  
 consisting of Br, Cl, and I; R<sup>1</sup> is independently alkyl,  
 alkene, aryl, alkoxy, aryloxy, amine, amide, fluoroalkyl,  
 fluoroaryl, alkyl ketone, aryl ketone, ester, formyl,  
 5 cyano, fluoro, imide, sulfone, and thioether; the X  
 halides are para to each other; and n = 0-4.

13. The method according to claim 1, wherein the  
 phosphite ligand has the formula:



- 15 wherein R<sup>2</sup>, R<sup>3</sup>, and R<sup>4</sup> are independently selected from the  
 group consisting of C<sub>3</sub> to C<sub>22</sub> alkyl, C<sub>6</sub> to C<sub>24</sub> aryl,  
 alkaryl, and aralkyl.

14. The method according to claim 10, wherein R<sup>2</sup>,  
 20 R<sup>3</sup>, and R<sup>4</sup> are independently selected from the groups  
 consisting of

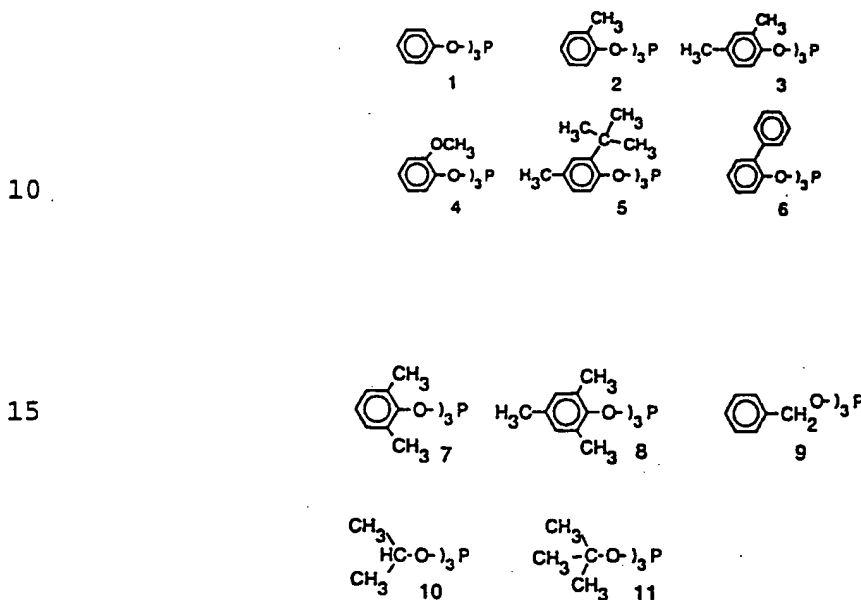


- 25  
 30 wherein A is independently selected from the group  
 consisting of C<sub>1</sub> - C<sub>22</sub> alkyl, C<sub>6</sub> - C<sub>18</sub> aryl, C<sub>1</sub> - C<sub>12</sub> alkoxy,  
 C<sub>6</sub> - C<sub>18</sub> aryloxy, and F, and wherein l = 0-5, m = 0-7, n =



1 0-9, and o = 0-21; the A groups can be on any of the fused  
or multiple rings; and q = 0-3.

5 15. The method according to claim 11, wherein the  
phosphite ligand is selected from the group consisting of:



25 16. The method according to claim 1, wherein the  
phosphite ligand is:



35 the nickel compound is nickel (II) chloride, and the  
reducing metal is zinc.

1           17. The method according to claim 1, wherein the  
aryl halide is 2,5 dichlorobenzophenone, the nickel  
compound is nickel (II) chloride, the phosphite is tri(2-  
5 methylphenyl)phosphite, the reducing metal is zinc, and  
the aprotic solvent is selected from the group consisting  
of N-methylpyrrolidinone (NMP), N,N-dimethylacetamide,  
N-cyclohexylpyrrolidinone, dimethylformamide, and N,N,N,N-  
tetramethylurea.

10           18. The method according to claim 1, wherein the  
aryl halide is N-(4-chloro-2-benzoylphenyl)succinimide,  
the aprotic solvent is NMP, the nickel compound is nickel  
(II) chloride, the phosphite is tri(2-  
15 methylphenyl)phosphite, and the reducing metal is zinc.

          19. The method according to claim 1, wherein the  
aryl halide is 4-chlorotoluene, the aprotic solvent is  
NMP, the nickel compound is nickel (II) chloride, the  
phosphite is tri(2-methylphenyl)phosphite, and the  
20 reducing metal is zinc.

          20. The method according to claim 1, wherein the  
aryl halide is 2-chlorobenzophenone, the aprotic solvent  
is NMP, the nickel compound is nickel (II) chloride, the  
25 phosphite is tri(2-methylphenyl)phosphite, and the  
reducing metal is zinc.

          21. The method according to claim 1, wherein the  
aprotic solvent is an amide solvent selected from the  
30 group consisting of N-methylpyrrolidinone, N,N-  
dimethylacetamide, N-cyclohexyl-pyrrolidinone, and  
dimethylformamide.

1           22. The method according to claim 2, wherein the  
chloride, bromide, and iodide ions are introduced as salts  
selected from the group consisting of alkali salts,  
alkaline earth salts, alkylammonium salts, aluminum salts,  
5           manganese salts, and zinc salts.

          23. The method according to claim 1, wherein the  
nickel compound is selected from the group consisting of  
nickel (II) chloride and nickel (II) bromide.  
10

          24. The method according to claim 1, wherein the  
phosphite ligand is an aryl phosphite.

          25. The method according to claim 1, wherein the  
15           phosphite ligand is tri-2-tolylphosphite.

          26. The method according to claim 1, wherein the  
phosphite ligand is triphenylphosphite.

20           27. The method according to claim 1, wherein the  
phosphite ligand is tri-(2,4-dimethylphenyl)phosphite.

          28. The method according to claim 1, wherein the  
phosphite ligand is tri-(2-methoxyphenyl)phosphite.  
25

          29. The method according to claim 1, wherein the  
phosphite ligand is tri-(2-tert-butyl-4-methyl-  
phenyl)phosphite.

30           30. The method according to claim 1, wherein the  
phosphite ligand is tri-(2-phenylphenyl)phosphite.

1           31. The method according to claim 1, wherein the  
aryl halide is 6-chloro-2-(4-fluorophenyl)-4-  
phenylquinoline.

5           32. The method according to claim 1, wherein the  
aryl halide is a protected form of 2-amino-4-  
chlorobenzophenone.

10           33. The method according to claim 1, wherein the  
aryl halide is 4-chloroacetophenone.

          34. The method according to claim 1, wherein the  
aryl halide is an aryl dihalide.

15           35. The method according to claim 1, wherein the  
aryl halide is 2,5-dichlorobenzophenone.

20           36. The method according to claim 1, wherein the  
aryl halide is 2,5-dichloro-4'-phenoxybenzophenone.

          37. The method according to claim 1, wherein the  
aryl halide is 2,5-dichlorobiphenyl.

25           38. The method according to claim 1, wherein the  
aryl halide is 2,4-dichlorobenzophenone.

30           39. The method according to claim 1, wherein the  
aryl halide is provided as a mixture of aryl dihalides,  
and the polyaryl product is a polyarene co-polymer.

- 1           40. The method according to claim 39, wherein one of  
the aryl dihalides has the formula:

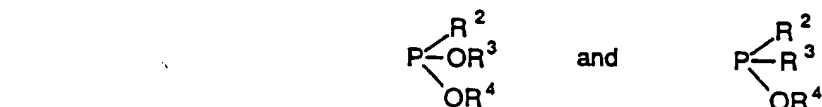


wherein X is independently selected from the group  
consisting of Br, Cl, and I; R¹ is independently alkyl,  
10 alkene, aryl, alkoxy, aryloxy, amine, amide, fluoroalkyl,  
alkyl ketone, aryl ketone, ester, formyl, cyano, fluoro,  
imide, sulfone, and thioether; the X halides are para to  
each other; and n = 0-4.

- 15           41. The method according to claim 1, wherein a  
mixture of two or more aryl halides is coupled.

20           42. A method of coupling aryl halides to form biaryl  
or polyaryl compounds, the method comprising the steps of:  
providing an aryl halide selected from the group  
consisting of an aryl chloride, an aryl bromide, an aryl  
iodide and mixtures thereof; and

contacting the aryl halide in an anhydrous  
aprotic solvent with a catalyst mixture comprising a  
25 nickel compound, a ligand selected from the group  
consisting of:



1 wherein R<sup>2</sup>, R<sup>3</sup>, and R<sup>4</sup> are independently selected from the  
group consisting of C<sub>1</sub> to C<sub>22</sub> alkyl, C<sub>6</sub> to C<sub>24</sub> aryl,  
alkaryl, and aralkyl, and a reducing metal to thereby form  
said biaryl or polyaryl compound.

5

43. A catalyst composition comprising a nickel  
compound, a phosphite ligand, and a reducing metal  
selected from the group consisting of aluminum, magnesium,  
and zinc, wherein the molar ratio of ligand to nickel is  
10 between 1 and 10, and the molar ratio of reducing metal to  
nickel is between 1 and 10,000.

44. The composition of claim 43, wherein the  
phosphite ligand is tri-2-tolylphosphite and the reducing  
15 metal is zinc.

45. The composition of claim 43, wherein the molar  
ratio of phosphite ligand to nickel is between 2 and 10.

20 46. The composition of claim 43, wherein said  
phosphite ligand is selected from the group consisting of  
triphenyl phosphite, tri-2,6-dimethylphenyl phosphite,  
tri-2-phenylphenyl phosphite, tri-2-methoxyphenyl  
phosphite, tri-n-butyl phosphite, tripentylphosphite,  
25 tribenzylphosphite, tri-isopropylphosphite, tri-2-tert-  
butylphenylphosphite, trinaphthylphosphite, tri-(2,4-  
dimethylphenyl)phosphite, tri-(2,4,6-trimethyl-  
phenyl)phosphite, and tri-(2-tert-butyl-4-methyl-  
phenyl)phosphite.

30

47. The composition of claim 43, wherein said  
phosphite is selected from the group consisting of tri C<sub>1</sub>-  
C<sub>22</sub> alkyl phosphites, tri C<sub>6</sub>-C<sub>24</sub> aryl phosphites,

35

1 triaryalkyl phosphites, and mixed alkyl, aryl, and  
aryalkyl phosphites.

48. A method of coupling aryl halides to form biaryl  
5 or polyaryl compounds, the method comprising the steps of:

a) providing an aryl halide selected from the  
group consisting of an aryl chloride, an aryl bromide, and  
an aryl iodide;

b) preparing a mixture comprising the aryl  
10 halide, a nickel compound or complex and a phosphite  
ligand in an anhydrous aprotic solvent containing an  
electrolyte;

c) placing the mixture in an electrochemical  
cell comprising a cathode; and

15 d) cathodically reducing the aryl halide to  
thereby form said biaryl or polyaryl compound.

49. A method of coupling aryl halides or aryl  
sulfonates to form biaryl or polyaryl compounds, the  
20 method comprising the steps of:

providing an aryl halide or aryl sulfonate  
selected from the group consisting of an aryl chloride, an  
aryl bromide, an aryl iodide, an aryl methanesulfonate, an  
aryl phenylsulfonate, an aryl tolylsulfonate, an aryl  
25 trifluoromethanesulfonate, an aryl fluorophenylsulfonate,  
and an aryl fluorosulfonate,; and

contacting the aryl halide or aryl sulfonate in  
an anhydrous aprotic solvent with a catalyst mixture  
comprising a nickel compound, a phosphite ligand, and a  
30 reducing metal to thereby form said biaryl or polyaryl  
compound.

## AMENDED CLAIMS

[received by the International Bureau on 4 October 1996 (04.10.96);  
original claims 1, 2, 42, 43, 48, and 49 amended;  
remaining claims unchanged (4 pages)]

1

1. A method of coupling aryl halides to form biaryl  
or polyaryl compounds, the method comprising the steps of:  
5 providing an aryl halide selected from the group  
consisting of an aryl chloride, an aryl bromide, and an  
aryl iodide; and

mixing the aryl halide in an anhydrous aprotic  
solvent with a nickel compound or a nickel complex, a  
10 phosphite ligand, and a reducing metal to thereby form  
said biaryl or polyaryl compound.

2. The method according to claim 1, wherein the  
catalyst mixture additionally comprises a promoter  
15 selected from the group consisting of chloride, bromide,  
and iodide salts is also mixed with the aryl halide.

3. The method according to claim 2, wherein the  
promoter is sodium iodide.  
20

4. The method according to claim 2, wherein the  
promoter is sodium bromide.

5. The method according to claim 1, wherein the  
25 phosphite ligand to nickel molar ratio is in the range of  
2 to 10.

6. The method according to claim 1, wherein the  
phosphite ligand to nickel molar ratio is in the range of  
30 2.4 to 5.

7. The method according to claim 1, wherein the  
reducing metal is selected from the group consisting of

35



- 1           40. The method according to claim 39, wherein one of  
the aryl dihalides has the formula:

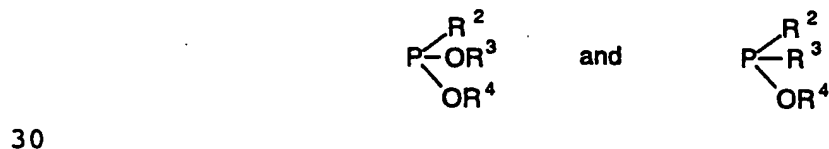


10 wherein X is independently selected from the group  
consisting of Br, Cl, and I; R<sup>1</sup> is independently alkyl,  
alkene, aryl, alkoxy, aryloxy, amine, amide, fluoroalkyl,  
alkyl ketone, aryl ketone, ester, formyl, cyano, fluoro,  
imide, sulfone, and thioether; the X halides are para to  
each other; and n = 0-4.

15

41. The method according to claim 1, wherein a  
mixture of two or more aryl halides is coupled.

20 42. A method of coupling aryl halides to form biaryl  
or polyaryl compounds, the method comprising the steps of:  
providing an aryl halide selected from the group  
consisting of an aryl chloride, an aryl bromide, an aryl  
iodide and mixtures thereof; and  
mixing the aryl halide in an anhydrous aprotic  
25 solvent with a nickel compound or nickel complex, a ligand  
selected from the group consisting of:



35

1 wherein R<sup>2</sup>, R<sup>3</sup>, and R<sup>4</sup> are independently selected from the  
group consisting of C<sub>3</sub> to C<sub>22</sub> alkyl, C<sub>6</sub> to C<sub>24</sub> aryl,  
alkaryl, and aralkyl, and a reducing metal to thereby form  
said biaryl or polyaryl compound.

5

43. A catalyst composition formed by mixing together  
in an anhydrous aprotic solvent a nickel compound, a  
phosphite ligand, and a reducing metal selected from the  
group consisting of aluminum, magnesium, and zinc, wherein  
10 the molar ratio of ligand to nickel is between 1 and 10,  
and the molar ratio of reducing metal to nickel is between  
1 and 10,000.

44. The composition of claim 43, wherein the  
15 phosphite ligand is tri-2-tolylphosphite and the reducing  
metal is zinc.

45. The composition of claim 43, wherein the molar  
ratio of phosphite ligand to nickel is between 2 and 10.

20

46. The composition of claim 43, wherein said  
phosphite ligand is selected from the group consisting of  
triphenyl phosphite, tri-2,6-dimethylphenyl phosphite,  
tri-2-phenylphenyl phosphite, tri-2-methoxyphenyl  
25 phosphite, tri-n-butyl phosphite, tripentylphosphite,  
tribenzylphosphite, tri-isopropylphosphite, tri-2-tert-  
butylphenylphosphite, trinaphthylphosphite, tri-(2,4-  
dimethylphenyl)phosphite, tri-(2,4,6-trimethyl-  
phenyl)phosphite, and tri-(2-tert-butyl-4-methyl-  
30 phenyl)phosphite.

47. The composition of claim 43, wherein said  
phosphite is selected from the group consisting of tri C<sub>3</sub>-

35

1 C<sub>22</sub> alkyl phosphites, tri C<sub>6</sub>-C<sub>24</sub> aryl phosphites,  
triaryalkyl phosphites, and mixed alkyl, aryl, and  
aryalkyl phosphites.

5 48. A method of coupling aryl halides to form biaryl  
or polyaryl compounds, the method comprising the steps of:  
providing an aryl halide selected from the group  
consisting of an aryl chloride, an aryl bromide, and an  
aryl iodide;

10 mixing together the aryl halide, a nickel  
compound or nickel complex and a phosphite ligand in an  
anhydrous aprotic solvent containing an electrolyte;

placing the mixture in an electrochemical cell  
comprising a cathode; and

15 cathodically reducing the aryl halide to thereby  
form said biaryl or polyaryl compound.

49. A method of coupling aryl halides or aryl  
sulfonates to form biaryl or polyaryl compounds, the  
20 method comprising the steps of:

providing an aryl halide or aryl sulfonate  
selected from the group consisting of an aryl chloride, an  
aryl bromide, an aryl iodide, an aryl methanesulfonate, an  
aryl phenylsulfonate, an aryl tolylsulfonate, an aryl  
25 trifluoromethanesulfonate, an aryl fluorophenylsulfonate,  
and an aryl fluorosulfonate,; and

mixing the aryl halide or aryl sulfonate in an  
anhydrous aprotic solvent with a nickel compound or nickel  
complex, a phosphite ligand, and a reducing metal to  
30 thereby form said biaryl or polyaryl compound.

## INTERNATIONAL SEARCH REPORT

International application No.  
PCT/US96/05378

## A. CLASSIFICATION OF SUBJECT MATTER

IPC(6) : C08G 61/10

US CL : 528/397; 502/162; 205/67

According to International Patent Classification (IPC) or to both national classification and IPC

## B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

U.S. : 528/397; 502/162; 205/67

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)

## C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	US, A 5,102,971 (HIMMLER ET AL) 07 April 1992, see the abstract.	1-48
A	US, A, 4,326,989 (COLON ET AL) 27 April 1982, see the abstract	1-48

☐ Further documents are listed in the continuation of Box C. ☐ See patent family annex.

* Special categories of cited documents:	"I"	later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention
"A" document defining the general state of the art which is not considered to be of particular relevance	"X"	document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone
"E" earlier document published on or after the international filing date	"Y"	document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art
"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)	"G"	document member of the same patent family
"O" document referring to an oral disclosure, use, exhibition or other means		
"P" document published prior to the international filing date but later than the priority date claimed		

Date of the actual completion of the international search

09 JULY 1996

Date of mailing of the international search report

15 AUG 1996

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